CLAIMS

1. A polypeptide comprising more than two ligand binding domains of a cytokine receptor wherein said domains are linked by a linker molecule and wherein the linker molecule comprises at least one proteolytic cleavage site.

2. A polypeptide according to claim 1 wherein said cleavage site is sensitive to a serum protease.

3. A polypeptide according to claim 2 wherein the serum protease is thrombin.

4. A polypeptide according to any of the preceding claims wherein said cleavage site comprises the amino acid sequence LVPRGS, or a variant thereof.

5. A polypeptide according to any of the preceding claims wherein said cleavage site comprises the amino acid sequence SGGGG, or a variant thereof.

6. A polypeptide according to any of the preceding claims wherein said cleavage site comprises the amino acid sequence PGISGGGGGG.

7. A polypeptide according to any of the preceding claims wherein said cleavage site comprises the amino acid sequence: LVPRGSPGISGGGGGG, or a variant thereof.

8. A polypeptide according to any of the preceding claims wherein said cleavage site comprises at least two copies of the amino acid sequence SGGGG, or a variant thereof, which flank said cleavage site.

9. A polypeptide according to any of the preceding claims wherein said polypeptide comprises at least four ligand binding domains.

10. A polypeptide according to claim 9 wherein said polypeptide has 4, 6, 8, 10, or 12 ligand binding domains.

11. A polypeptide according to any of the preceding claims 1 to 8 wherein said polypeptide has 3, 4, 5, 6, 7, 8, 9, or 10 ligand binding domains.

12. A polypeptide according to any of the preceding claims 1 to 9 wherein said polypeptide has greater than 10 ligand binding domains.

13. A polypeptide according to any of the preceding claims wherein said polypeptide is an antagonist.

14. A polypeptide according to any of the preceding claims wherein said polypeptide is an agonist.

15. A polypeptide according to any of the preceding claims wherein said cytokine receptor ligand binding domain is selected from the ligand binding domains of the cytokines selected from the group consisting of: growth hormone; leptin; erythropoietin; prolactin; interleukins (IL), IL-2, IL-3, IL-4, IL-5, IL-6, IL-7, IL-9, IL-10, IL-11; the p35 subunit of IL-12, IL-13, IL-15; granulocyte colony stimulating factor (G-CSF); granulocyte macrophage colony stimulating factor (GM-CSF); ciliary neurotrophic factor (CNTF); cardiotrophin-1 (CT-1); leukaemia inhibitory factor (LIF); oncostatin M (OSM); interferon, IFNα and IFNγ.

16. A polypeptide according to claim 15 wherein the binding domain is the ligand binding domain of growth hormone.

17. A polypeptide according to claim 16 wherein the binding domain is the ligand binding domain of leptin.

18. A polypeptide according to any of the preceding claims wherein the linker is a polypeptide which comprises from 5 to 50 amino acid residues.

19. A polypeptide according to claim 18 wherein the linker comprises from 5 to 30 amino acid residues.

20. A polypeptide according to any of the preceding claims wherein the linker comprises at least one copy of the peptide Gly Gly Gly Gly Ser.

21. A polypeptide according to claim 20 wherein the linker is 5 amino acids in length and consists of one copy of the (Gly4Ser) linker.

22. A polypeptide according to claim 20 wherein the linker is 10 amino acids in length and consists of two copies of the (Gly4Ser)2 linker.

23. A polypeptide according to claim 20 wherein the linker is 15 amino acids in length and consists of three copies of the (Gly4Ser) linker.

24. A polypeptide according to claim 20 wherein the linker is 20 amino acids in length and consists of 4 copies of the (Gly4Ser)4 linker.

25. A polypeptide according to any of the preceding claims wherein the polypeptide is a fusion protein comprising inframe translational fusions of ligand binding domains.

26. A polypeptide according to any of the preceding claims comprising chemical crosslinkers wherein the chemical crosslinkers serve to link the ligand binding domains.

27. A polypeptide according to claim 26 wherein the chemical crosslinker comprises a homo-bifunctional crosslinker selected from the group consisting of; disuccinimidyl-suberimidate-dihydrochloride; dimethyl-adipimidate-dihydrochloride; 1,5,-2,4 dinitrobenezene.

28. A polypeptide according to claim 26 or claim 27 wherein the crosslinker comprises a hetero-bifunctional crosslinker selected from the group consisting of; N-hydroxysuccinimidyl 2, 3-dibromopropionate; 1-ethyl-3-[3-dimethylaminopropyl] carbodiimide hydrochloride; succinimidyl 4-[n-maleimidomethyl]-cyclohexane-1-carboxylate.

29. A nucleic acid molecule comprising a nucleic acid sequence which encodes a polypeptide according to any of the preceding claims.

30. A nucleic acid molecule comprising the sequence selected from the group consisting of:

(i) the sequence represented by Figs 4 or 6;

(iii)a sequence which hybridises to the sequence of (i) above and which has cytokine receptor modulating activity; and

(iii)a sequence which is degenerate as a result of the genetic code to the sequences defined in (i) and (ii) above.

31. A nucleic acid molecule which hybridises under stringent hybridisation conditions to the sequences represented in Figs 4 or 6.

32. A polypeptide encoded by the nucleic acid molecule according to any of claims 29 to 31.

33. A polypeptide according to claim 32 wherein said polypeptide is modified by deletion, addition, and/or substitution of at least one amino acid residue and said modification enhances the antagonistic or agonistic effects of said polypeptide with respect to the inhibition or activation of receptor mediated cell signalling.

34. A vector including a DNA molecule wherein said DNA molecule encodes a polypeptide according to any of claims 1 to 28, 32 or 33.

35. A vector according to claim 34 wherein said vector is an expression vector adapted for prokaryotic or eukaryotic gene expression.

36. A vector according to claim 34 or 35 wherein said vector encodes, and thus said recombinant polypeptide is provided with, a secretion signal to facilitate purification of said polypeptide.

37. A method to prepare a polypeptide according to any of claims 1 to 28, 32 or 33 comprising;

(i) growing a cell transformed or transfected with a nucleic acid of any of claims 29 to 31 or a vector of claims 34 to 36 in conditions conducive to the manufacture of said polypeptide; and

(ii) purifying said polypeptide from said cell, or its growth environment.

38. A cell transformed/transfected with the vector of claims 34 to 36 or the nucleic acid of claims 29 to 31.

39. Use of the polypeptide of any of claims 1 to 28, 32 or 33 and/or the nucleic acid of claims 29 to 31 and/or the vector of claims 34 to 36 as a pharmaceutical.

40. A pharmaceutical composition comprising the polypeptide according to any of claims 1 to 28, 32 or 33, and/or the nucleic acid of claims 29 to 31 and/or the vector of claims 34 to 36 wherein said pharmaceutical optionally comprises a carrier, excipient and/or a diluent.

41. Use of the polypeptide of any of claims 1 to 28, 32 or 33 and/or the nucleic acid of claims 29 to 31 and/or the vector of claims 34 to 36 for the manufacture of a medicament for the treatment of a disease wherein said disease is selected from the group consisting of: acromegaly; gigantism; GH deficiency; Turners syndrome; renal failure; osteoporosis; diabetes mellitus; cancer; obesity; insulin resistance; hyperlipidaemia; hypertension; anaemia; autoimmune and infectious disease; inflammatory disorders including rheumatoid arthritis.

42. A method of treating a human or animal subject comprising administering an effective amount of the polypeptide of claims 1 to 28, 32 or 33, and/or the nucleic acid of claims 29 to 31 and/or the vector of claims 34 to 36 and/or the pharmaceutical composition of claim 40 and/ or the medicament of claim 41 to said subject.